apparatus involves both mass spectrometry and ion mobility spectrometry. That is, as described in much more detail in the Amendment dated June 26, 2003, the present invention provides for two-dimensional separation, in which the first separation step involves ion mobility spectrometry, and the second step involves mass spectrometry.

In addition to the usual advantages of two-dimensional separation, the combination of the present invention provides an additional advantage. That is, one of the disadvantages of time-of-flight mass spectrometers is that they inherently require pulsed intermittent operation. Once a pulse of ions has been injected into the flight tube of the mass spectrometer, it is necessary to wait until all of the ions in the sample have traveled the length of the flight tube and been detected before injecting the next pulse. Otherwise, late arriving ions from a previous pulse may contaminate a reading taken for a subsequent pulse. The need to wait until all of the ions have cleared the flight tube results in a poor duty cycle, particularly where the sample of ions has a wide m/z ratio.

One of the advantages of combining IMS with mass spectrometry is that there is an approximate correspondence between ion behavior and the two separation steps. Thus, in both IMS and low pressure mass spectrometry, a heavy ion will take longer to traverse the instrument due to a large m/z ratio. That is, a heavy ion will take longer to pass through a low pressure mass spectrometer, and will also have a low mobility resulting in a large drift or transit time through an IMS device. As a result, lighter ions will pass through the IMS device more quickly, while heavier ions take a longer time. This provides grouped input to the mass spectrometer, in which the faster ions are provided first and the m/z ratio range for each pulse or group is reduced as the IMS device has already separately grouped, to some extent, ions having widely different m/z ratios. This reduces the waiting period for each group of ions, as ions in the same group will have similar m/z ratios and will thus take similar lengths of time to traverse the mass spectrometer. This, in turn, improves the duty cycle of the mass spectrometer.

To some extent, ion output from the IMS must be modified before being accepted by the downstream low pressure mass spectrometer. That is, the diameter of the ion beam exiting the IMS section is much larger than the acceptance of the low pressure mass spectrometer as radial spread of the ion beam is inherent in the nature of IMS. Without modification, the resolution or sensitivity of a high performance, low pressure mass spectrometer would also be compromised.

Prosecution History

Much of the prosecution of this patent application has centered on whether it is obvious to provide an RF ion guide between the IMS and the downstream low pressure mass spectrometer to focus the ion beam exiting the IMS. In the first office action dated February 26, 2003, the Examiner took the position that the subject matter covered by some of the claims was unpatentable over the combined teachings of Clemmer and United States patent No. 5,572,035 (Franzen).

Clemmer discloses a hybrid mobility-mass spectrometry apparatus involving both IMS and mass spectrometry. The diameter of the ion beam exiting the cell taught by Clemmer is much larger than the acceptance of the orthogonal time-of-flight analyzer. Clemmer attempts to narrow the ion beam by focusing the beam using ion optics in the form of a DC lens (Figure 4, reference No. 47).

In the first office action, the Examiner cited Franzen as disclosing the suitability of RF multipole rod systems as ion guides for transporting ions between ion production and ion consumption devices, particularly in feeding mass spectrometers of any type. The Examiner then took the position that it would have been obvious to modify the teachings of Clemmer by replacing the DC lens with the RF multipole rod system taught by Franzen.

In our response to the first office action, we pointed out that there are well known problems with the approach taken by Clemmer to narrow the ion beam downstream from the IMS. Despite these problems, no one had thought to replace the DC lens taught by Clemmer with the RF multipole rod system taught by Franzen. Reasons for this were readily apparent from reviewing references in the art. In our response we quoted from some of these references to support our contention that there is an understanding in the art that to use an RF ion guide as a focusing device will limit the resolution of the mobility spectrometer, as the RF ion guide will tend to "stretch" out the ion beam, thereby counteracting the tendency of the IMS device to provide a pulsed ion output.

From the recent office action dated October 3, 2003, it initially appeared that the Examiner had accepted the above argument, as the Franzen reference was dropped from the Examiner's argument. Instead, the Examiner relies on the teachings of Russ IV et al. However, exactly the same argument seems to apply with respect to the teachings of Russ IV et al. as applied with respect to the teachings of Franzen. That is, it is respectfully submitted that it would not have been obvious to replace the DC lens taught by Clemmer with the RF ion guide devices taught by either Franzen or Russ IV et al. due to the understanding in the art that to use an RF ion guide as a focusing device will limit the resolution of the mobility spectrometer, as the RF ion guide will tend to "stretch" out the ion beam, thereby counteracting the tendency of the IMS device to provide a pulsed ion output.

Detailed Reply to Claim Rejections

As noted by the Examiner, Russ IV et al. discloses using a ring pole ion guide apparatus between mass spectrometer stages. The Examiner takes the position that Russ IV et al. discloses the suitability of using a ring pole ion guide apparatus between mass spectrometer stages to (1) focus the ions, and (2) provide a collision cell. The Examiner then appears to take the further position that the teachings of Russ IV et al. regarding the suitability of the ring pole ion guide apparatus for these two purposes provides the necessary motivation to modify the Clemmer d vice by replacing the DC

lens taught by Clemmer with the ring pole ion guide taught by Russ IV et al. For the reasons that follow, this position is respectfully traversed.

In the response to the first office action, we pointed to two papers and one patent to show that there is an understanding in the art that to use a RF ion guide as a focusing device will limit the resolution of the mobility spectrometer. This point applies to the outstanding office action as well. In general, it remains our position that the use of an RF ion guide to focus an ion beam received from a mobility spectrometer would not have occurred to those skilled in the art as they would have concluded that the RF ion guide would counteract the tendency of the IMS to provide a pulsed ion output.

Yes, Russ IV et al. teach the use of an ring pole ion guide. However, they do not teach the use of an RF ion guide downstream from an IMS. The shared understandings of those skilled in the art would militate against using an RF ion guide to focus an ion beam downstream from an IMS as this would tend to "stretch" out the ion beam, thereby counteracting the tendency of the IMS device to provide a pulsed ion output. Thus, it would be unobvious to one of skill in the art, given the teachings of Clemmer and Russ IV et al., to use an RF ion guide to focus an ion beam downstream from an IMS. That this is the case can be inferred from the fact that neither Clemmer nor Russ IV et al. nor Thomson nor Smith teach the use of an RF ion guide for the purpose of focusing and maintaining the temporal spacing of ions between an ion mobility section and a mass analyzer section in a hybrid mobility-mass spectrometry apparatus despite the known problems with the Clemmer device resulting from its reliance on the DC lens.

This remains the case even given the suitability of the ring pole ion guide apparatus for other purposes. That is, the fact that Russ IV et al. teach that the ring pole ion guide is suitable to both focus the ions and to function as part of a collision cell, does not affect the understanding of those skilled in the art that an RF ion guide would tend to counteract the tendency of the IMS to provide a pulsed ion output, thereby reducing the efficacy of the hybrid mobility-mass spectrometry apparatus.

Based on the foregoing, it is respectfully submitted that claims 1, 16, 29 and 33 are unobvious over the teachings of the patents cited. That is, the subject matter covered by all of these claims involves an RF ion guide that generates a field to promote focusing of ions in the radial dimension along the axis of the RF ion guide. The use of an RF ion guide for this purpose is not taught in the prior art cited, nor is it consistent with the teachings of the prior art generally, which teachings indicate that an RF ion guide is unsuitable for this purpose as it will tend to spread out the pulses emitted by the IMS.

In view of the foregoing, it is respectfully submitted that claims are allowable over the cited references. Allowance of the application is respectfully requested.

If any questions arise, it is requested that the undersigned be contacted at the number provided below.

Respectfully submitted,

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